REMARKS/ARGUMENTS

This is in response to the Office Action mailed December 27, 2005 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Applicants have amended claims 1 and 6 to overcome the rejection under 35 USC § 112, second paragraph. Claims 11-15 have been added corresponding to claims 1-5, with limitations specific to treatment of humans.

Claims 1 and 6 stand rejected under 35 USC § 112, first paragraph, as lacking written description. The issues unique to claim 6 have been overcome by amendment. The Examiner argues that "while the specification provides adequate written description for antisense oligonucleotides and siRNA targeted to human clusterni, the full breadth of non-nucleic acid inhibitors of human clusterin and inhibitors of any-type directed to clusterin of any species other than human" is not described by an adequate written description.

This written description rejection is of the new, second type, which has recently emerged in court decisions, rather than the older "new matter" type of rejection. This second type of rejection has recently been described by the Court of Appeals for the Federal Circuit as follows:

> The second application of the written description requirement is reflected in *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). There, this court invoked the written description requirement in a case without priority issues.
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> More recently, in *Enzo Biochem*, we clarified that *Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure. Amgen, 314 F.3d at 1332.
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> The test for compliance with §112 has always required sufficient information in the original disclosure to show that the inventor possessed the invention at the time of the original filing. See *Vas-Cath*, 935 F.2d at 1561 ("Adequate description of the invention guards against the inventor's overreaching by insisting that he recount his invention in such detail that his future claims can be determined to be encompassed within his original creation"). The possession test requires assessment from the viewpoint of one of skill in the art. Id. at 1563-64 ("the applicant must ... convey with reasonable clarity to those skilled in the art that, as

> of the filing date sought, he or she was in possession of the invention") (emphasis in original); *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000) ("The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed'") (citation omitted).

The focus of the written description requirement is therefore plainly on the **invention**, that is the contribution made by the inventors. The new face of the written description requirement is not intended to limit claims to the specific examples of the invention set forth in the specification, or to prevent claim scope that includes embodiments or improvements that may be developed later by the inventors or others. Stated differently, the written description requirement does not not impose a burden to invent all the foreseeable variations and/or improvements prior to filing.

Applicants have discovered that reduction of clusterin is of therapeutic benefit in the treatment of non-cancerous angiogenesis-related disease. What the Examiner is arguing is that to protect the full scope of their invention and copying of Applicants' discovery using other types of therapeutic agent, Applicants are required to test and discover every conceivable method for performing the methods of the invention. In the absence of such extensive research conducted prior to filing of the application, the Examiner says that the claims must be limited to the genus of the specific examples, leaving the Applicants at the mercy of every copyist who chooses to steal their invention by using some different active agent than antisense or siRNA. Applicants are aware of no such burden imposed by the law of the United States. Thus, the rejection should be withdrawn.

The Examiner also rejected claims 1-3 and 6-8 under 35 USC § 112, first paragraph as lacking enablement, stating that enablement was only provided for reduction of clusterin expression using antisense agents *in vitro*. In support of this rejection, the Examiner cites various generalized articles commenting on challenges facing antisense as a therapeutic *in vivo*. The arguments made relate to antisense generally, and do not address and specific reasons why the statements made in the present application that the invention does work are not credible to persons skilled in the art. Applicants enclose a copy of a declaration filed in a related case, Serial No. 09/967,726, in which clinical trials of an antisense targeted to clusterin are reported. While these trials are preliminary and directed to toxicity assessment, it is apparent that no special carrier was required to achieve *in vivo* reduction of clusterin expression in cancer cells of varying types and locations whose common characteristic was the overexpression of clusterin. Since angiogenesis is also associated with increased clusterin expression, and since the present application shows that reduction of clusterin expression reduces angiogenesis, the teaching of the application is reasonably enabling and therefore sufficient.

The Examiner rejected claims 6 and 7 as anticipated by US Patent No. 6,383,808 of Monia; claims 6-8 as anticipated by Gleave et al. WO 00/49937, claims 6-8 as anticipated by US 6,900,187 of Gleave et al., and claims 6-8 as anticipated by US 2003/0158130 of Gleave et al. In each case, the Examiner has acknowledged that the reference says nothing about reducing angiogenesis, but the examiner argues that this is not required because the active method step is the same. Applicants respectfully disagree with this assessment of the scope of the claims which ignores most of the words of the claim and the application of the art.

The words that the Examiner is failing to take into account are not located only in the preamble. Nevertheless, case law on preamble language is instructive. The Court of Appeals for the Federal Circuit has recently observed that

> "In general, a preamble limits the [claimed] invention if it recites essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim." Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 808, 62 USPQ2d 1781, 1784 (Fed. Cir. 2002) (quoting Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999)). "[A] claim preamble has the import that the claim as a whole suggests for it. In other words, when the claim drafter chooses to use both the preamble and the body to define the subject matter of the claimed invention, the invention so defined, and not some other, is the one the patent protects." Bell Communications Research, Inc. v. Vitalink Communications Corp., 55 F.3d 615, 620, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995).

Eaton Corp. v. Rockwell International Corp., 66 USPQ2d 1271 (Fed. Cir. 2003). In the present case, the ignored language cannot be deemed superfluous, since it says what is being accomplished by the method, namely a reduction in angiogenesis, and the claim without these words is meaningless. Indeed, the notion that preamble language is generally meaningless in method claims would render second use method claims impossible.

The importance of the preamble in method claims of this type is reflected in *Jansen v. Rexall Sundown, Inc,* 68 USPQ 2d 1154 (Fed. Cir. 2003). In that case, the claims at issue were directed to "a method of treating or preventing macrocytic-megaloblastic anemia" by administration of a composition of defined components "to a human in need thereof." The accused product was a dietary supplement having a composition as defined in the claims. It was lableled for uses that did not include treating or preventing macrocytic-megaloblastic anemia. The Federal Circuit found that the claims were limited to the use, as stated in the preamble. Similarly, in *Rapoport v. Dement*, 59 USPQ2d 1215 (Fed. Cir. 2001) a claims directed to "a method for treatment of sleep apneas" was interpreted as being just that, and not a method for treating symptoms associated with sleep apneas, which was found in the art.

In *Jansen* the Federal Circuit observed that

> in both *Rapoport* and this case, the claim preamble sets forth the objective of the method, and the body of the claim directs that the method be performed on someone 'in need.' In both cases, the claims' recitation of a patient or a human 'in need' gives life and meaning to the the preambles' statement of purpose. The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method is performed.

Jansen at 1158. In this case, claim 6 is directed to "a method for reducing angiogenesis in a non-cancerous angiogenesis-related disease." Treatment is given to "cells associated with a non-cancerous angiogenesis-related disease" and the result is an reduction in angiogenesis. These recitations are equivalent to the "in need" statements of *Jansen* and *Rapoport*. The acknowledged absence of disclosure of angiogenesis reduction in the cited reference is therefore fatal to an anticipation rejection, and the rejections should be withdrawn.

For these reasons, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully submitted,

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Enclosure:

copy of 132 declaration from 09/967,726

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Gleave, et al. Application No.: 09/967,726 Filed: 9/28/2001 Title: Chemo-and Radiation-sensitization of Cancer by Antisense TRPM-2 Oligodeoxynucleotides Attorney Docket No.: UBC.P-022 Customer No.: 021121	Group Art Unit: 1635 Examiner: Tracy Ann Vivlemore Confirmation No: 6881

Commissioner for Patents

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DECLARATION UNDER RULE 132

The undersigned each hereby declare as follows:

1. I am a named inventor of the above-captioned application. As such, I am familiar with the application, including the claims.

2. This declaration is submitted to set forth results from clinical trials that have been conducted since the filing of the application.

3. This declaration is signed by less than all of the inventors, because the other inventors, H. Miyake and T Zellweger, are no longer associated with the project, and have had no involvement, and thus no personal knowledge of the trials reported here.

4. Limited clinical testing (two Phase I studies) has been conducted to evaluate toxicity of OGX-011, an antisense oligonucleotide that has the sequence as set forth in Seq. ID NO.: 4 of the above-captioned application. The oligonucleotide is modified as described in Application Serial No. 10/080,794. A total of 25 patients with localized prostate cancer with high risk features were enrolled in the first study. In the second study, a total of 30 patients suffering from renal cancer, non-small cell lung cancer, ovarian cancer, peritoneal cancer or prostate cancer were enrolled, each of whom was refractory to one or more prior treatment regimens.

5. In both phase I studies, antisense treatments were made at levels of 40, 80, 160, 320, 480 or 640 mg and administered intravenously 3 times during the first week, and once a week thereafter. In the first phase I study, antisense therapy was combined with concurrent hormone ablation therapy for 5 weeks prior to radical prostatectomy. Concentrations of OGX-011 in prostate tissue and of TRPM-2 mRNA and protein in prostate and lymph node tissue were determined. At all levels of antisense, dose-dependent reduction in levels of TRPM-2 mRNA was observed in the lymph nodes of the patients treated, and in laser captured, micro-dissected prostate cancer levels, indicating that all of the amounts of antisense tested had a measurable affect at the expression level. The amount of TRPM-2 in serum also decreased in a dose-dependent manner.

6. This study established a dose of 640 mg as the recommended dose based on safety, tolerability, and tissue levels of antisense and TRPM-2 mRNA and/or protein.

7. In the second Phase I study, two schedules of concurrent docetaxel treatment were evaluated: 30 mg/m^2 weekly or 75 mg/m^2 every three weeks. Of 18 patients with measurable disease, the interim response rate (the study is still in progress) was 38.9%, including 33.3% with stable disease, and 5.6% achieving an objective partial response.

8. Two ovarian cancer patients showed reductions in the measured amount of the tumor marker CA125. In one patient receiving 160 mg OGX-011, the amount of CA125 marker decreased from 19,600 to 4720 over 71 days after commencement of treatment. In another who received 480 mg OGX-011, the marker level decreased from 2000 before treatment to around five hundred after 33-44 days. A slight increase to around 900 was observed during a second treatment cycle. Other patients with ovarian cancer had low initial CA125 and so a decrease could not be evaluated.

9. Two prostate cancer patients showed reduction in the amount of PSA tumor marker. In one patient receiving 40 mg OGX-011, the PSA level decreased from 90 prior to therapy to 35 after 4 treatment cycles at approximately 45 day intervals, and remained at 56 at a later date. In a second patient receiving 320 mg OGX-011, the PSA level dropped from a pre-treatment level of 1478 to a level of about 425 after 4 cycles of treatment.

10. The selection of initial dosages for this study was consistent with standard protocols for clinical trials to evaluate toxicity, and no experimentation was needed to arrive at dosage levels that produced observable reduction in TRPM-2 mRNA or serum TRPM-2.

11. While the data in this study is preliminary and difficult to draw many conclusions from because of the small sample size, the number of variables that were considered, including prior treatment of the patients, and the short duration of the test, several conclusions can be drawn. Standard

protocols for trial design were used and arrived, without experimentation, at working levels for antisense dosing that produced reduction in TRPM-2 mRNA and serum TRPM-2 without significant toxicity, and this treatment in combination with docetaxel produced beneficial results in patients who had been refractory to prior treatment.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

dated: April 6/05

Martin Gleave

dated: April 5/05

Paul Rennie

dated: April 5/05

Colleen Nelson